have very little understanding of the relationship between the structure of a regulatory network and its dynamical nature. In this study we introduce a new mathematical method, named "linkage logic", to analyze dynamics of network systems. By this method, we can restrict possible steady states of a given complex network system only from the knowledge of regulatory linkages. We formalize two aspects of the linkage logic: "principle of compatibility", determines the upper limit of the degree of freedom of steady-state diversity realized by a given network. "Principle of dependency", determines the possible combinations of states of the system. By combining these two, (1) for a given network, we can identify a cluster of nodes which reflect possible steady states of the whole system, (2) we can reduce a given complex network into a simpler one without loss of the ability to generate the diversity of steady states, (3) we can examine the consistency between the structure of network and observed set of steady states, and (4) sometimes we can predict unknown states or unknown regulations only from observed set of steady states. We illustrate the method by several applications to experimentally determined regulatory networks, including gene network for early development of ascidian and the regulatory network of signal transduction pathway.

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SRY function in sex determination

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Male sex determination in mammals is regulated by SRY, a single copy gene on the Y chromosome. In inherited sex reversal families the father and the daughter share the same SRY. Here, we investigate one such inherited case, V60L. This mutation is located in the minor wing of DNA-binding HMG box. Biochemical studies demonstrated near-native DNA interaction. However, cell-culture studies of the rodent gonadal cell model indicated a partially impaired nuclear localization. The compatibility of the V60L SRY with either male (father) or female (daughter) development may reflect polymorphisms in genes affecting the efficiency of nuclear import. We next investigated the major wing of the SRY HMG box. Whereas the V60L mutation demonstrated that remodeling of the minor wing can be tolerated in nuclear import, we sought to ask if the structure of the major wing is likewise adaptable. A probe is provided by the mutations with unstructured HMG box. Upon rescue of nuclear localization signal, the double mutants exhibit substantial gene-regulating activity. These results highlight the importance of specific DNA-directed protein folding in the assembly of sex-specific transcription regulating complexes. To study further testicular differentiation, we have investigated the nuclear export of SRY. I90M, another inherited clinical father–daughter mutation, located in Nuclear Export Signal and perturbs its function. We propose that nucleocytoplasmic shuttling regulates phosphorylation of SRY, which in turn modulates specific DNA binding. Together, we generate a cascade model of SRY in male-determination, and it also shows that our model highly correlates protein characters with their roles in development biology.

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